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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/586,479	06/01/2000	Alexander C. Schmidt	15280-414000US	8296

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 11/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/586,479	SCHMIDT ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *84-163* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *84-163* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 September 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application. This application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid. Applicant's submission filed on August 26, 2005 has been entered. The cancellation of claims 1-83 renders all previous rejections of claims 1-83 moot.

New claims 84-163 are pending and under examination. Previously, claims to polynucleotides, vectors and methods of using the polynucleotides were restricted out. However, upon further consideration, the restriction requirement is withdrawn in an effort to examine this application in a consistent manner with other applications of the same family.

Claim Objections

2. Claims 153-157 are objected to for misspelling the term, "infectious".

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 84, 85, 87, 89-96, 99-104, 117, 118, 119, 121, 123-130, 133-137 and 150-152 are rejected under 35 U.S.C. 102(e) as being anticipated by Belshe *et al* (5,869,036). The claims are drawn to an infectious human-bovine chimeric parainfluenza virus (PIV) comprising a major nucleocapsid protein (N), a nucleocapsid phosphoprotein (P), a large polymerase protein (L), and a partial or complete chimeric human PIV3 (HPIV3)-bovine PIV3 (BPIV3) genome or antigenome that comprises at least one gene segment(s) encoding an open reading from of a HN or F gene of a human PIV, said gene segment(s) being operably linked to regulatory sequences operable in said chimeric PIV genome or antigenome; said infectious chimeric PIV being attenuated for replication at least 10-fold in the respiratory tract of a primate host compared to wild type HPIV3. In a particular embodiment, the chimeric virus contains the wild-type L protein of the vector PIV.

Belshe teaches an isolated *cp*45 hybrid virus (a derivative of HPIV-3 JS) which is suitable for use as a vaccine in humans and animals comprising nucleic acid encoding nucleocapsid protein, phosphoprotein, at least one surface antigen of a target virus, and large polymerase protein (cols. 2-3). The target virus must have an envelope and one or more surface antigens or surface glycoproteins, such as HPIV-1, HPIV-2 and RSV. Belshe discloses that the gene sequence which encodes the surface glycoproteins of the target virus may be substituted for the corresponding sequence in the *cp*45 genome which codes for the HN and F proteins, to result in a chimeric genome (cols. 8-9). For example, Belshe teaches that bovine RSV and cattle PIV-3 are target viruses whose surface glycoproteins may be substituted into the cp45 genome (col. 8, lines 54-58).

Other viruses include RSV (F and G proteins), influenza, measles (HN and F protein), HIV and others (col. 8, lines 42-58). Attenuating mutations are introduced into the L segment as well as other proteins (col. 5, lines 42-67 and col. 6, lines 1-3). Belshe teaches that the cp45 genome has an amino acid substitution at Leu992 in the L protein. Also disclosed is the production of hybrid virus with a wild type L protein that is also attenuated (col. 8, lines 21-25). Belshe says the chimeric PIV can be used in a vaccine, or immunogenic composition, comprising a physiologically acceptable carrier (column 2, lines 32-33).

Regarding the limitation about regulatory sequences, one would expect that regulatory sequences were present in Belshe's construct because virus was produced. Therefore, the invention as claimed is anticipated by Belshe.

Response to Arguments

4. Applicant's observations and arguments are primarily directed to the following:

- Applicant discloses that the recovery of Belshe's hybrid *cp*45 viruses was performed by a complementation assay wherein a plasmid expressing wild-type HPIV3 L protein provided a very small degree of recovery of virus plaques.
    - In response to this observation, the examiner agrees that the viruses were recovered. Regardless of the amount recovered, Belshe did recover virus (col. 8, lines 21-25). The claims do not require a particular amount of virus be produced.
- Applicant points out that Belshe's explanation for attenuation is mutation of the L protein, not the wild-type. Applicant asserts that Belshe does not contemplate any attenuated virus obtained by mutating other than the L protein. In contrast, Applicant's

claims are directed to embodiments wherein the L protein is the wild-type, and the virus remains attenuated due to other temperature-sensitive mutations.

- In response to this observation, Example 5 of the Belshe patent discloses the introduction of the wild type L gene into the *cp*45 genome. Belshe recovered virus that contained a wild type L gene and also contained mutation in gene other than the L gene. Because the *cp*45 genome necessarily contains mutations in other genes besides the L gene, the introduction of the wild type L gene resulted in a virus that expressed the wild type L protein along with the other mutations that are naturally present in the *cp*45 virus.

- Applicant argues that Belshe only uses the HPIV cp45 genome or antigenome, having at least two of the three defined point mutation in the L protein to obtain an attenuated HPIV3 virus. Applicant notes that Belshe suggests that an attenuated HPIV3 virus might be modified by substitution of its genes encoding the HN and/or F glycoproteins with the corresponding genes from a target virus, among those listed in col. 8, lines 42-58. Applicant asserts that the method with which to accomplish this suggestion by Belshe is not disclosed whatsoever.

  - The complex method to which Applicant is referring to is not present in the claims. Belshe's method of producing viruses is the same as that instantly claimed: cell culture. The method steps of the instant claims include expressing the polynucleotide genome in a cell culture. Belshe teaches the same method (col. 8, lines 21-25).

- Applicant argues that the instant chimeric genome achieves a host range attenuation phenotype, even in the absence of the L gene mutations (at positions 942, 992, 1558). Applicant argues that Belshe's embodiments require mutations in the L gene in order to recover an attenuated hybrid virus. In contrast, Applicant's claims are directed to embodiments wherein the L protein is the wild-type, and the virus remains attenuated due to other temperature-sensitive mutations.
    - In response to this observation, Example 5 of the Belshe patent discloses the introduction of the wild type L gene into the *cp*45 genome. Belshe recovered virus that contained a wild type L gene and also contained mutation in gene other than the L gene. Because the *cp*45 genome necessarily contains mutations in other genes besides the L gene, the introduction of the wild type L gene resulted in a virus that expressed the wild type L protein along with the other mutations that are naturally present in the *cp*45 virus.
- Applicant argues that Belshe does not provide the concept of inserting the heterologous gene encoding an open reading frame between the background regulatory sequences. Applicant argues that Belshe discloses only the entire gene, coding portions taken together with the regulatory portions.
    - In response to this assertion, the claims read on both HPIV3 and BPIV3 regulatory sequences. According to the claims, either sequence may be used because they are recited in the alternative. Therefore, if Belshe teaches the substitution of the entire gene including the start and end sequences, the claim

limitation has been met by Belshe because the substituted BPIV-3 sequences include the gene start and end sequences.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 84-163 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 144-215 of copending Application No. 09/083,793. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is encompasses the embodiments set forth in the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. Claims 84-163 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 53-85 of copending Application No. 09/458,813. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is encompasses the embodiments set forth in the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Claims 84-163 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-30 and 46-74 of copending Application No. 09/459,062. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is encompasses the embodiments set forth in the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 84-163 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 180-222 of copending Application No. 09/733,692. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is a species of the instantly claimed genus of PIVs, rendering the genus claims obvious.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

9. No claim is allowed.

Claims 86, 88, 120 and 122 recite limitations regarding incorporation of the N (nucleocapsid) gene from BPIV3 into the HPIV genome. Claims 97, 98, 131 and 132 recite limitations regarding the incorporation of the P (phosphoprotein) gene from BPIV3 into the HPIV genome. Belshe does not teach or fairly suggest the substitution of these proteins from heterologous viruses, specifically BPIV3. Belshe teaches the substitution of surface glycoproteins that are involved in attachment, penetration and/or release.

Claims 105-116, 138-149 and 153-163 are drawn to human-bovine chimerics wherein a supernumerary gene of an additional virus is incorporated into the genome. Belshe does not contemplate such an embodiment. Belshe teaches incorporating genes from another target virus into the human PIV-3 genome, resulting in a human-bovine chimeric. Belshe does not teach or fairly suggest the addition of yet another gene to the human-bovine chimeric.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Stacy B. Chen
November 14, 2005